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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/523,927	02/07/2005	Hana Stepankova	264288US0PCT	1890

22850 7590 12/21/2007  
OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.  
1940 DUKE STREET  
ALEXANDRIA, VA 22314

EXAMINER
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NAGUBANDI, LALITHA

ART UNIT	PAPER NUMBER
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1621

NOTIFICATION DATE	DELIVERY MODE
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12/21/2007

ELECTRONIC

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com  
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jgardner@oblon.com

<b>Office Action Summary</b>	<b>Application No.</b> 10/523,927	<b>Applicant(s)</b> STEPANKOVA ET AL.	
	<b>Examiner</b> Lalitha Nagubandi	<b>Art Unit</b> 1621	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 07 February 2005.
- 2a) ☐ This action is FINAL. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-12 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-12 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>7<sup>th</sup> Feb 2005</u> | 6) <input type="checkbox"/> Other: _____  |

***Detailed Action***

***Status of the Claims***

Claims 1-12 are pending. Claims 1- 12, are considered for examination in this office action.

***Specification***

The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

***Claim Rejections - 35 USC § 102***

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States

Claims 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Ciszewska et al ( Journal of Labelled Compounds and Radiopharmaceuticals vol. XXXIX, No. 8 pages 651 - 668).

Applicants' claim a method of production of (-) – (S) -3-[1-(dimethylamino)ethyl]phenyl-N-ethyl-N-methylcarbamate of formula **II** or of its hydrogentartrate of formula **I**, comprising, reductive aminating methoxyacetophenone of formula **VI** to form the compound of formula **V** which

is de-alkylated to the racemic amine of formula **IV** and is further resolved to the compound of formula **III**. Compound of formula **III** is reacted with compound of formula **VII**, as embodied in claim 1.

Ciszewska et al disclose, the instant process from methoxy [<sup>14</sup>C]acetophenone ( please see compound 14, page 655 and follow the sequence of the steps from compound 14 through compound 4) resulting in rivastigmine hydrogentartrate. The instant claim has been rejected based on the fact that the claiming of the instant process is inherently present in the prior art although it is not explicitly taught by using the unlabelled compounds as claimed in the instant application. However, the process has given enough direction on page 654, line 20-22, that using unlabeled system would lead to better yields.

Thus the instant claim is rejected based on the fact that, the claiming of a new use, new function or unknown property which is *inherently* present in the prior art does not necessarily make the claim patentable. *In re Best*, 562 F.2d 1252, 1254, 195 USPQ 430,433 (CCPA 1977). *In re Crish*, 393 F.3d 1253, 1258,73 USPQ 2d 1364, 1368 (Fed. Cir. 2004), The court states that “ just as the discovery of properties of a *known material* does not make it novel, the identification and characterization of a prior art material also does not make it novel”. Please see MPEP 2112.

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 1-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ciszewska et al ( Journal of Labelled Compounds and Radiopharmaceuticals vol. XXXIX, No. 8 pages 651 - 668) and in view of MacDonald et al (J Chem Soc, 1932, 2513-2519) .

Applicants' claim a method of production of (-) – (S) -3-[1-(dimethylamino)ethyl]phenyl-N-ethyl-N-methylcarbamate of formula **II** or of its hydrogentartrate of formula **I**, comprising, reductive aminating methoxyacetophenone of formula **VI** to form the compound of formula **V** which is de-alkylated to the racemic amine of formula **IV** and is further resolved to the compound of formula **III**. Compound of formula **III** is reacted with compound of formula **VII**, as embodied in claim 1.

Further, in the dependent claims applicants' claim the resolution of the compound of formula **IV** by reacting with S (+) camphor 10 sulfonic acid.

**Determination of the scope and content of prior art**

Ciszewska et al teach, the instant process from methoxy [<sup>14</sup>C]acetophenone ( please see compound 14, page 655 and follow the sequence of the steps from compound 14 through compound 4) resulting in rivastigmine hydrogentartrate.

MacDonald et al teach ( see page 2514, lines 17-22 and also see the whole document) the resolution of m-hydroxy phenylethylmethanamine using bromo camphor sulphonic acid.

**Ascertainment of difference between the prior art and the claims**

The difference between the prior art and in the instant claims is that Ciszewska et al teach rivastigmine hydrogentartrate containing C-14 labelled compounds, whereas the instant claims embodies unlabelled compounds. Further, the dependent claims use camphor sulfonic acid as the resolving agent to resolve compound of formula IV to compound of formula III.

Camphor sulfonic acids have been used as the resolving agents specifically for the resolution of m-hydroxyphenylethylmethanamine by MacDonald.

**Finding of prima facie obviousness-rationale and motivation**

The examiner contends that it would have been obvious to have used unlabelled carbon compounds in the process of Ciszewska as the process has given enough direction on page 654, line 20-22, that using unlabeled system would lead to

better yields. Moreover, it would have been obvious to combine the resolution techniques taught by MacDonald in the process of Ciszewska with a reasonable expectation of success of resolving the compound of formula IV.

It is a routine practice in the field of synthetic chemistry to alter the nature of the starting material specifically in the instant case, based on the availability of the isotopic abundance of the unlabelled organic substrate, cost and stability and an ordinary artisan would have had a reasonable expectation of success to obtain the instant compounds as embodied in the instant claims.

### ***Conclusion***

No claims are allowed

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Lalitha Nagubandi whose telephone number is 571 272 7996.

The examiner can normally be reached on 6.30am to 3.30pm. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne, Eyler can be reached on 571 272 0871. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Lalitha Nagubandi  
Patent Examiner  
Technology Center 1600

December 17<sup>th</sup>, 2007.



Samuel A Barts

Primary Patent Examiner  
Technology Center 1600